Higher-than-expected severe (Grade 3-4) late urinary toxicity after postprostatectomy hypofractionated radiotherapy: a single-institution analysis of 1176 patients.


Abstract

BACKGROUND: Dose escalation and hypofractionation may have a role in postprostatectomy radiotherapy (RT), but at the risk of increasing urinary toxicity.

OBJECTIVE: To address predictors of severe (Grade ≥3) late urinary toxicities (LGUTOX3) after postoperative irradiation.

DESIGN, SETTING, AND PARTICIPANTS: A single-institution cohort of 1176 patients treated between 1993 and 2010 with adjuvant or salvage RT was analyzed. A total of 929 patients underwent conventionally fractionated (CF) RT (1.8 Gy per fraction; median dose to the prostatic bed: 70.2 Gy) with nonconformal RT (n=169), three-dimensional conformal RT (n=657), or intensity-modulated RT (n=103) technique, while 247 patients received hypofractionated helical TomoTherapy (median: 2.50 Gy per fraction) at the following doses: 117 patients at 65.8 Gy (2.35 Gy in 28 fractions), 80 patients at a median of 71.4 Gy (2.5-2.6 Gy in 28 fractions), and 50 patients at 58 Gy in 20 fractions. Total doses were converted into 2 Gy-equivalent doses (EQD2) following the linear quadratic model taking α/β=5.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Univariable and multivariable Cox regression models tested the relationship between clinicodosimetric variables and the risk of LGUTOX3 retrospectively, graded according to Common Terminology Criteria for Adverse Events v.4.0.

RESULTS AND LIMITATIONS: After a median follow-up of 98 mo, the 5-yr risk of LGUTOX3 was 6.9% and 18.1% in the CF and hypofractionated cohorts, respectively. At univariable analysis, the risk of LGUTOX3 was predicted by dose per fraction (hazard ratio [HR]: 2.96), acute Grade ≥2 toxicity (HR: 2.37), EQD2, pT4, and year of irradiation. At multivariable analyses, acute Grade ≥2 toxicity and dose per fraction independently predicted LGUTOX3 in the population, while an interaction analysis indicated a predictive role of hypertension in the hypofractionated cohort only. These findings are limited by their retrospective nature.

CONCLUSIONS: In the postprostatectomy setting, the logistic convenience of hypofractionation should be carefully balanced against the risk of severe late urinary sequelae.

PATIENT SUMMARY: This study investigated the causes of urinary adverse effects after postprostatectomy radiotherapy. Hypofractionation resulted in an increased risk of severe urinary toxicities.

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